THE SIGNIFICANCE OF LUNG UPTAKE OF Tc-99m HMPAO IN ONLY CIGARETTE SMOKERS, AND PATIENTS WHO ARE BOTH CIGARETTE SMOKERS AND ALCOHOL ABUSERS

Sadece sigara içenlerde ve sigara ile birlikte alkol kullananlarda Tc-99m-HMPAO'nın akciğer tutulumunun önemi

Ahmet Tutuş[1], Mustafa Kula[2], Mehmet Nardalı[2], Güler Silov[2], Tacettin Yolcu[2], Seher Sofuoğlu[3]

Summary: *Tc-99m HMPAO, a lipophilic cyclic amine used as a brain SPECT imaging, has been reported to localize in smoker's lungs. Thirty-nine patients referred to our department for brain imaging for psychiatric disorders underwent lung imaging studies immediately following the brain imaging to quantitate lung uptake and to determine the relation between the lung uptake of the tracer and the use of alcohol. The patients were divided into three groups: Group I, non-smokers (n=17), Group II, smokers (n=12), and Group III, smokers and alcohol abusers (n=10). The smokers had been smoking from 4-47 years, and daily cigarette consumption ranged from 10-40 cigarettes. Anterior lung images including the whole of the lungs and upper part of the liver were taken at 45th minute after intravenous injection of 555 MBq of Tc-99m HMPAO. The mean lung/liver ratios were calculated with the uptake of radiotracer in the regions of interest which were drawn over the liver and lung. The mean lung/ liver ratios for group I, group II, and group III were 0.443±0.021, 0.602±0.030, and 0.816± 0.057, respectively. There are statistically differences among the groups (p< 0.001). These results suggest that there is a significantly higher Tc-99m HMPAO pulmonary uptake in smoker and alcohol abusers expressed by higher lung/ liver activity ratio than in the teetotallers.*

Key Words: *Tc-99m HMPAO, Cigarette smoking, Alcohol abuse*

Özet: *Beyin perfüzyon görüntülemesinde kullanılan ve lipofilik siklik amin yapısında olan Tc-99m HMPAO'nun sigara içenlerin akciğerlerinde tutulduğu bildirilmiştir. Bu tutulumu ölçmek ve alkol kullanımıyla ilişkisini saptamak amacıyla psikiyatrik hastalık nedeniyle beyin görüntülemesi için müracaat eden 39 hastanın akciğer görüntüleri alındı. Hastalar sigara içmeyen 17, sigara içen 12 ve sigara ile birlikte alkol kullanan 10 hasta olmak üzere üç gruba bölündü. Sigara içenlerde günlük sigara tüketimi 10-40 adet ve sigara içme süreleri 4-47 yıl arasındaydı. 555 MBq Tc-99m-HMPAO'nun intravenöz verilmesini takiben 45. dakikada tüm akciğerleri ve karaciğerin üst bölümünü içine alan anterior toraks görüntüleri alındı. Akciğer ve karaciğer üzerinden alınan ilgi alanlarından akciğer/karaciğer oranları hesaplandı. Gruplar için hesaplanan ortalama oranlar sırasıyla 0.443±0.021, 0.602±0.030 ve 0.816± 0.057 olarak bulundu. Tüm grupların oranları arasında istatiksel olarak anlamlılık mevcuttu (p< 0.001). Bu sonuçlar sigara ve alkol içenlerde, içmeyenlerden daha belirgin Tc-99m-HMPAO tutulumu olduğunu göstermektedir*

Anahtar Kelimeler: *Tc-99m HMPAO, Sigara kullanımı, Alkol kötüye kullanımı*

Tc-99m HMPAO, a lipophilic cyclic amine, exhibits the ability to pass through the blood-brain barrier and to localize permanently in normal brain tissue (1-3). This agent is widely used for the diagnosis of strokes, dementia and schizophrenia.

Erciyes Üniversitesi Tıp Fakültesi 38039 KAYSERİ
Nükleer Tıp. Y.Doç.Dr.[1], Araş.Gör.Dr.[2]. Psikiyatri. Prof.Dr. [3].

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Pulmonary uptake of 99mTc-HMPAO in two individuals has been previously reported (4). However, there has been no pulmonary localization except in the lungs of smokers (4,5). Factors influencing heart and lung uptake of ^{99m}Tc-HMPAO are still unknown (4).

Chronic alcoholism is responsible for morphologic alterations virtually in all organs and tissues in the

body, particularly in the liver and stomach (6). But, there are few reports of alcohol-induced pathological changes in lungs. We could not encounter any reports about ^{99m}Tc-HMPAO uptake in the lungs of alcohol abusers. Most alcoholics are also smokers. Therefore, we intended to obtain a lung/liver uptake ratio to evaluate pulmonary localization of ^{99m}Tc-HMPAO and its relation between alcohol using and cigarette smoking.

Since ^{99m}Tc-HMPAO is normally taken up by the liver, we have utilized a lung/liver uptake ratio to evaluate pulmonary localization of ^{99m}Tc-HMPAO and its relation to alcohol using associated with cigarette smoking.

MATERIAL AND METHODS

Thirty-nine patients (27 male, 12 female; range 18-70 yr.) who were referred to our department for ^{99m}Tc-HMPAO brain imaging studies for major depression, strokes or alcohol withdrawal syndrome underwent this investigation. The patients were divided into three groups. Group I, non-smoking teetotallers were defined as those who had never smoked and taken alcohol on daily basis (n= 17, age: mean±SEM = 40.36± 11.45). Group II, smokers were defined as those who had smoked cigarettes on daily basis (n= 12, age: mean±SEM = 36.41± 7.76). Group III, smokers and alcohol abusers were defined as those who had smoked cigarettes and drunk alcohol on daily basis (n= 10, age: mean±SEM 38.7± 8.11). The smokers had been smoking from 4-47 years, and their daily cigarette consumption ranged from 10-40 cigarettes. All of the alcoholic patients were smokers and had been using alcohol from 5-25 years.

No patients had any major systemic disease and none of them used any other drug except alcohol. All the subjects had laboratory findings (serum electrolytes, liver function tests, kidney function tests, urinanalysis, CBC, ECG) within the normal limits and physical examinations were normal. The plain chest films showed no abnormality suggesting inflammation or space occupying lesions. But in some smokers, there were the presence of minimal increased pulmonary vasculature. Pulmonary function tests cannot be performed because of technical reasons. Informed consent was obtained from each patient before starting the study.

Anterior lung images, 5 min per view, were taken at 45th minute after intravenous injection of 555 MBq (15 mCi) of ^{99m}Tc-HMPAO. The images including whole of the lungs and upper part of the liver were obtained using single-headed rotating gamma camera (Toshiba GCA 602 A/ SA, Tokyo, Japan), equipped with a low-energy all purpose collimator interfaced to Toshiba Computer System. The uptake of radiotracer in the regions of interest over the midportion of the right lung and the right upper part of the liver were drawn and calculated to obtain lung/ liver ratios. Histories of both cigarette smoking and alcohol intake, including duration and daily consumption, were recorded.

Statistical comparisons were made by One Way Analysis of Variance. Scheffe procedure was used for post ANOVA test. P value less than 0.05 was considered to be statistically significant.

RESULTS

Pulmonary distribution of ^{99m}Tc-HMPAO is usually unimportant in the nonsmoker patients (Fig.1). Figure 2 is an anterior image of cigarette smoking patient showing average radioactivity in the lungs, and the lung activity is higher than that of the heart. Figure 3, smokers' and alcohol abusers' anterior lung images, shows diffused and marked radiotracer localization in the lungs. The clinical details of study groups are shown in Table 1-3. The duration of smoking is up to 47 years, daily cigarette consumption ranged from 10-40 cigarettes. These data did not correlate with lung/liver uptake ratio. The statistical results of the lung/liver uptake ratios in three groups are shown in Table 4. The difference among the mean uptake ratios of all groups was statistically significant ($F=29.426$, $p< 0.001$).

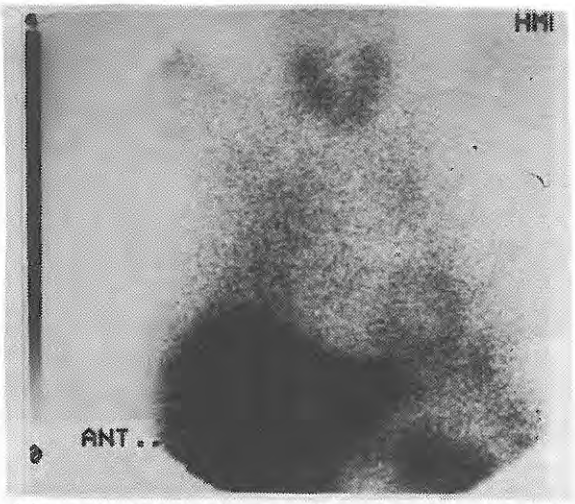

Figure 1. Anterior image of a non-smoker's chest-abdomen. There is absent radioactivity in the lungs, faint radioactivity in the heart, and marked radioactivity in the liver.

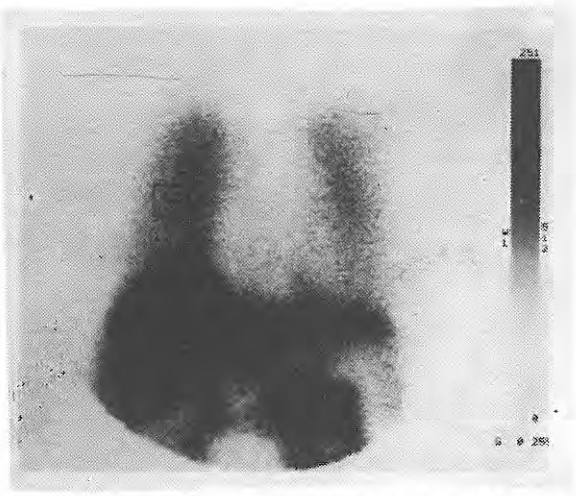

Figure 2. Anterior image of a smoker's chest-abdomen. There is average radioactivity in the lungs, but higher than in the heart. Regions of interest of the lung and liver.

Table 1. The lung/liver uptake ratios in the nonsmoking teetotallers

No	Sex/ Age	Lung/ Liver Uptake Ratios
1	F/ 23	0.39
2	F/ 70	0.59
3	F/ 59	0.33
4	M/ 40	0.54
5	F/ 32	0.51
6	F/ 66	0.51
7	M/ 47	0.37
8	F/ 59	0.40
9	M/ 45	0.34
10	M/ 35	0.39
11	F/ 42	0.35
12	M/ 65	0.47
13	M/ 54	0.40
14	F/ 18	0.40
15	M/ 37	0.52
16	M/ 33	0.41
17	M/ 54	0.61

Table 2. The lung/liver uptake ratios and clinical details of the smoking patients

No	Sex/ Age	Lung/ Liver Uptake Ratio	No. of Daily Cigarette	Duration of Smoking (yr)
1	M/ 43	0.59	20	20
2	M/ 39	0.83	30	24
3	M/ 41	0.66	20	25
4	M/ 60	0.64	20	47
5	F/ 39	0.75	40	24
6	M/ 30	0.59	30	15
7	M/ 45	0.55	20	15
8	M/ 23	0.52	30	8
9	F/ 31	0.51	20	6
10	M/ 41	0.52	15	20
11	M/ 26	0.58	15	4
12	M/ 32	0.48	20	15

Table 3. The lung/liver uptake ratios and clinical details of the smoking patients with alcohol abuse

No	Sex/ Age	Lung/ Liver Uptake Ratio	No of Daily Cigarette	Duration of Smoking (yr)	Duration of Alcohol Using (yr)
1	M/ 30	0.47	15	10	5
2	M/ 43	0.91	20	15	15
3	F/ 32	0.77	20	15	10
4	M/ 35	0.89	30	14	12
5	M/ 46	1.09	20	25	20
6	M/ 24	0.85	40	10	6
7	F/ 41	0.73	20	22	15
8	M/ 43	0.72	20	30	13
9	M/ 50	0.69	15	30	8
10	M/ 43	1.04	20	20	25

Table 4. The comparison of the mean lung/ liver uptake ratios in the groups studied

Groups	n	Lung/ Liver Uptake Ratio Mean±SEM
Group-I	17	0.443±0.021
Group-II	12	0.602±0.030
Group-III	10	0.816±0.057
	F=29.426	P< 0.001

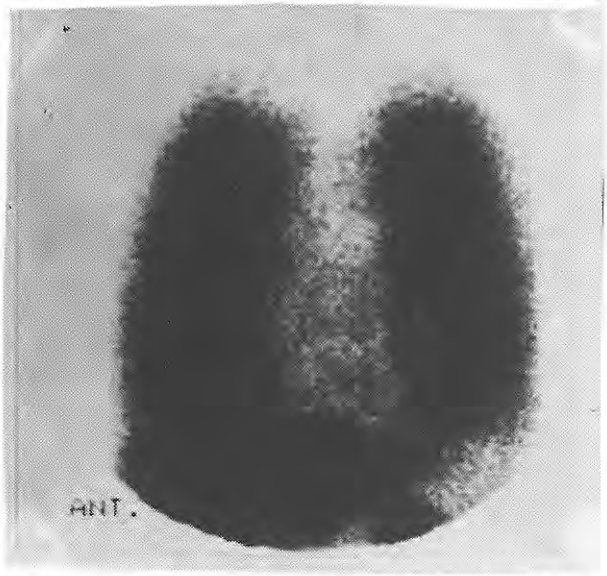

Figure 3. Anterior image of chest-abdomen of a smoker with alcohol user's. There is diffusely and markedly increased uptake of radiotracer in the lungs.

DISCUSSION

These results indicate that there is a significantly high ^{99m}Tc-HMPAO pulmonary uptake expressed by a high lung/liver activity ratio in smoker patients with alcohol abuse. Besides, cigarette smokers as a group have significantly higher lung/liver uptake of ^{99m}Tc-HMPAO compared to patients who have never smoked, and this finding is in agreement with the results in Shih's, et al (7,8). The smoking questionnaire also solicited information on smoking technique (depth inhalation, brand of cigarette) but no meaningful correlation with lung/ liver uptake was found. Nevertheless, our findings are concordant with Shih's, et al animal study (9) in documenting significantly high lung uptake in the smoke-exposed subjects.

Tc-99m HMPAO is a lipophilic brain imaging agent, its uptake in the liver and excretion through the hepatobiliary route is significant (14% to 30%) (1). Pulmonary localization has been observed only in the lungs of smokers and in almost all those patients who had pulmonary emphysema with a past history of smoking (7,8). However it is still unknown which factors will determine the degrees of lung uptake. Its site of localization seems presumably in the pulmonary vascular endothelium

(10,11). Postulated mechanisms for increased ^{99m}Tc-HMPAO uptake in the smoker's pulmonary vascular endothelial cells include the following; smoking induced neutrophil stasis in the lung and release of smoking-associated mediators such as carbon monoxide, nicotine, nitrogen oxide, tar and formalin lead to changes of pulmonary endothelial cell function (12,13).

The contribution of cigarette smoking to disease is well summarized in a recent report of the U.S. Department of Health and Human Services "Today cigarette smoking is recognized as the single most preventable cause of death in our society, and the most important public health issue of our time" (14). Hazards of smoke include risk of lung cancer, heart disease, stroke, and emphysema (15). The best parts of cigarette smoking are the benefits derived from quitting; for example, a man or woman who quits smoking may have a decline in the risk of coronary heart disease, particularly myocardial infarction (16). Early objective documentation of the effects of smoking on the lung may helpful in convincing a patient to stop smoking. The pulmonary uptake of ^{99m}Tc-HMPAO as an indicator of smoke exposure may provide early diagnosis of lung injury due to smoking.

Most alcoholics are also smokers. Chronic alcoholism is responsible for morphologic alterations virtually in all organs and tissues in the body, particularly in the liver and stomach (6). Acetaldehyde, a major oxidative metabolite of ethanol, is very reactive compound and has been proposed as the mediator of the widespread tissue and organ damage. Although the catabolism of acetaldehyde is more rapid than that of alcohol: Chronic ethanol consumption raises the blood level of acetaldehyde by reducing the oxidative capacity of the liver augmented by the habituated drinker (17). In this study, all the subjects had laboratory findings (serum electrolytes, liver and kidney function tests, urinanalysis, CBC, ECG) within the normal limits.

Since we have not distinct alcohol user population, we get into difficulty in the evaluation of pulmonary localization of ^{99m}Tc-HMPAO in the lungs of the alcohol abusers. Nevertheless, we could not encounter any report about ^{99m}Tc-HMPAO uptake in the lungs of the alcohol users. It is clear that regular alcohol intake has an increasing effect on the ^{99m}Tc-HMPAO uptake in the smoker's lungs. This increasing effect is probably related to increased vascular permeability. It may also be related to adverse effects of chronic alcoholism. Does regular alcohol intake make a patient predisposed to lung uptake? Can pulmonary uptake decrease after the cessation of regular alcohol taking? These issues should be further investigated.

Pulmonary function tests, although not differentiating between anatomical emphysema and other causes of airflow obstruction, are noninvasive and reliable in predicting functional impairment (18). In this study, pulmonary function tests cannot be performed because of technical reasons. Tc-99m HMPAO lung imaging may serve as an additional or alternative diagnostic modality. This imaging may complement existing pulmonary function testing, Xe-133 ventilation imaging, and ^{99m}Tc MAA perfusion imaging. Whether this imaging is more sensitive than pulmonary function tests or other diagnostik modalities in detecting lung injury in association with cigarette smoking is subject to further study.

In conclusion, there is significantly higher ^{99m}Tc-HMPAO uptake expressed by higher lung/liver ratio in cigarette smokers with alcohol abuse compared both to smoking patients without alcohol abuse and non-smoking teetotalers. Early objective documentation of the effects of smoking on the lung may be helpful in convincing a patient to stop smoking. The pulmonary uptake of ^{99m}Tc-HMPAO may serve as an additional or alternative way to detect lung injury due to smoking.

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